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Indirect Electroreductive Cyclization and Electrohydrocyclization Using Catalytic Reduced Nickel(II) Salen

James A. Miranda, Carolyn J. Wade, and R. Daniel Little*

Department of Chemistry & Biochemistry, University of California Santa Barbara, Santa Barbara, California 93106

little@chem.ucsb.edu

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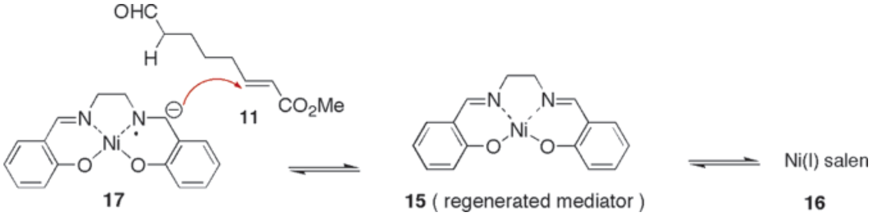

We describe efforts to achieve the electroreductive cyclization (ERC) and the electrohydrocyclization (EHC) reactions using catalytic nickel(II) salen as a mediator. While nickel(II) salen proved effective, the analogous cobalt complex as well as nickel(II) cyclam were not. The transformations were achieved in yields ranging from 60 to 94% using either a mercury pool or an environmentally preferable reticulated vitreous carbon (RVC) cathode. These examples represent the first instances wherein a nickel salen complex has been used in this manner. Clear differences between the voltammetric behavior of the ERC and EHC substrates were observed. The bisenoate **14**, for example, displays a substantially larger catalytic current. When the structurally modified mediator **31** was used, the electron-transfer pathway shuts down. Instead, the reduced form of **31** behaves as an electrogenerated base, leading to the formation of the intramolecular Michael adduct **23**. Presumably, the methyl groups of the modified ligand diminish the ability of the reduced form of the complex to serve as a nucleophile but not as a base. Aldehyde **23** was also characterized as a side product of the nickel(II) salen mediated electroreductive cyclization of **11**. Given that it is absent from nonmediated processes, its formation is linked to the presence of the mediator. To account for the results, we favor the existence of a mechanistic continuum involving an equilibrium between nickel(II) salen (**15**) and two reduced forms, one being the metal-centered species **16**, the other being a ligand-centered species **17**. We postulate that one form may be more prominently involved with the chemistry than another, depending upon the electronic properties/requirements of the substrate, and suggest that the equilibrium will shift to accommodate the need. Thus, for a hard electrophile like an alkyl halide, the properties of **16** ought to dominate, whereas **17** ought to predominate as the reactive species accounting for the chemistry described herein since it properly matches a soft ligand-centered nucleophile with a soft electron deficient alkene.

Introduction

There are many reactions that can be and have been referred to as "electroreductive cyclizations".[1] We have applied the acronym "ERC" to those processes wherein an electron-deficient alkene that is tethered to an acceptor (e.g., an aldehyde or ketone) undergoes an electrochemically promoted reductive cyclization leading to the formation of a new sigma bond between the β-carbon of the alkene and the acceptor unit in the manner illustrated in Scheme 1.[2]

Since the reaction first appeared in the literature, several nonelectrochemical variants have been devised,

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[1] (a) Little, R. D.; Moeller, K. D. *Electrochem. Soc. Interface* **2002**, *11* (4), 36–42. (b) Little, R. D.; Schwaebe, M. K. Reductive cyclizations at the cathode. In *Electrochemistry VI: Electroorganic Synthesis: Bond Formation at Anode and Cathode*; Steckhan, E., Ed.; Topics in Current Chemistry 185; Springer: Berlin, 1997; pp 1–48.

[2] (a) Little, R. D.; Fox, D. P.; Van Hijfte, L.; Dannecker, R.; Sowell, G.; Wolin, R. L.; Moëns, L.; Baizer, M. M. *J. Org. Chem.* **1988**, *53* (10), 2287–94. (b) Enholm, E. J.; Cottone, J. S. O-Stannyl Ketyl Radicals. In *Radicals in Organic Synthesis*; Renaud, P., Sibi, M. P., Eds.; Wiley-VCH: Weinheim, Germany, 2000; Vol. 2, Chapter 3.4, pp 221–232 and references therein. (c) Molander, G. A. Samarium(II) Mediated Radical Reactions. In *Radicals in Organic Synthesis*; Renaud, P., Sibi, M. P., Eds.; Wiley-VCH: Weinheim, Germany, 2000; Vol. 1, Chapter 2.1, pp 153–182 and references therein.

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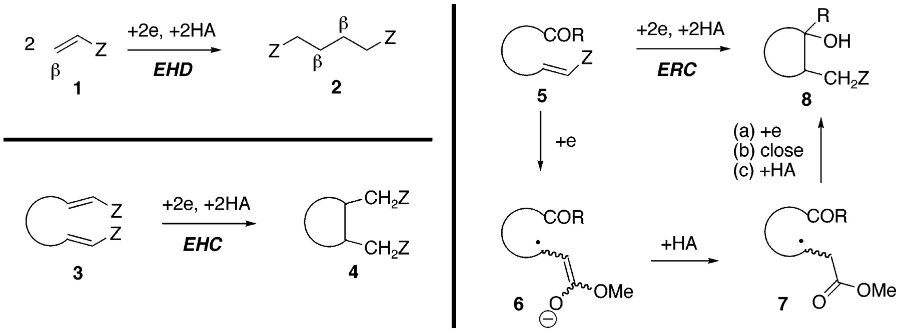
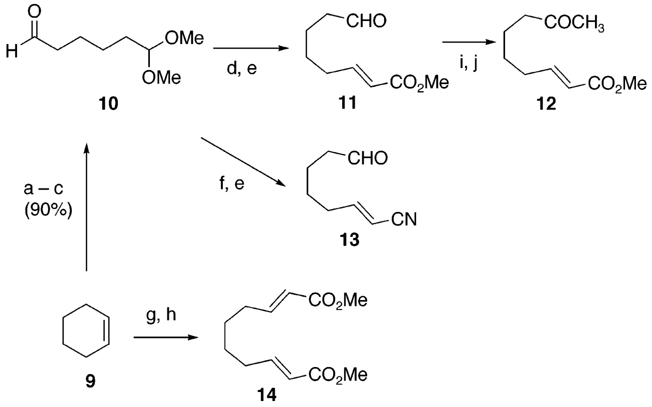
SCHEME 1. Schematic Formulations of the EHD, EHC, and ERC Reactions



most notably those involving the use of one electron reductants tributyltin hydride and samarium diiodide.[2b,c] Other intriguing variations use catalytic $Ni(COD)_2$ in the presence of diethylzinc,[3] vanadium (II),[4] Mg in methanol,[5] and Zn/TMSCl [6] to list a few. We believe that existence of a reasonable number of variants attests, in part, to the importance of the bond construction. Indeed, we and others have used it in the total synthesis of a variety of natural products.[2b,c,7] The electrochemical variant of the ERC reaction has been the subject of a detailed mechanistic investigation which concluded that the order of events is[8] (1) addition of the first electron to form a radical anion, (2) a rate-determining protonation followed by (3) the addition of a second electron and then (4) cyclization and finally (5) a second protonation (Scheme 1).[8]

The electrohydrocyclization (EHC; Scheme 1) reaction first appeared in the literature in 1966.[9] It was developed in Baizer's group at Monsanto as a spin-off of studies conducted there involving the electrochemical *β*,*β*-coupling of acrylonitrile (electrohydrodimerization or EHD; Scheme 1), a process rendered exceptionally important by its utility in the production of Nylon 6-6. Both the EHC and EHD reactions have been the subject of intense study for many decades.[10] Once again, nonelectrochemical variants have appeared, and once again those using butyltin hydride, samarium diiodide, and catalytic $Ni(COD)_2$/diethylzinc have become important variants.[2b,c,3]

SCHEME 2. Synthesis of Substrates 11−14[a]



[a] (a) O_3, −78 °C, $MeOH/CH_2Cl_2$; (b) cat TsOH; (c) Me_2S, rt (80% for steps a−c); (d) $Ph_3P{=}CHCO_2Me$, CH_2Cl_2, rt; (e) CF_3CO_2H, CH_2Cl_2/H_2O (1:1.2, v/v), 12 h rt (77% combined yield for steps d and e); (f) NaH, $(EtO)_2POCH_2CN$, THF, 0 °C (78%, steps f and e); (g) O_3, −78 °C, CH_2Cl_2; (h) $Ph_3P{=}CHCO_2Me$, MeOH, −78 °C to room temperature (30%, two steps); (i) MeLi, THF, −78 °C, 3 h (>95%); (j) SO_3·pyr, DMSO, 0 °C (53%).

In 1975, Lund and Simonet described the electrochemically mediated EHD of monoactivated olefins.[11] The reduced form of several aromatic and heteroaromatic compounds proved to be suitable electron-transfer agents. Variable amounts of catalytic current (vide infra) were observed in the cyclic voltammograms, the value being a function of the activated olefin and mediator that was selected.

In this manuscript, we describe our efforts to affect the ERC and EHC reactions electrocatalytically and our successes to date, and we offer a mechanistic rationale for the chemistry that has been uncovered thus far.

Synthesis of Starting Materials. Four substrates, **11**−**14**, were investigated. Each was synthesized by following the routes illustrated in Scheme 2.[2a,12] Assembly of the EHC substrate **14** was particularly straightforward since the ozonide produced from cyclohexene (**9**) could simply be treated directly with 2 equiv of the stabilized ylide to afford **14**.[13]

Selection of a Mediator. To achieve electrocatalysis, we deemed it necessary to use a redox mediator, a

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(3) (a) Wang, L.-C.; Jang, H.-Y.; Roh, Y.; Lynch, V.; Schultz, A. J.; Wang, X.; Krische, M. J. *J. Am. Chem. Soc.* **2002**, *124* (32), 9448−9453. (b) Montgomery, J.; Oblinger, E.; Savchenko, A. V. *J. Am. Chem. Soc.* **1997**, *119* (21), 4911−4920. (c) Mahandru, G. M.; Liu, G.; Montgomery, J. *J. Am. Chem. Soc.* **2004**, *126* (12), 3698−3699. (d) Montgomery, J. *Angew. Chem., Int. Ed.* **2004**, *43* (30), 3890−3908. (e) Cossy, J. *Bull. Chim. Soc. Fr.* **1994**, *131* (3), 344−56.

(4) Inokuchi, T.; Kawafuchi, H.; Torii, S. *J. Org. Chem.* **1991**, *56* (16), 4983−5.

(5) Lee, G. H.; Choi, E. B.; Lee, E.; Pak, C. S. *J. Org. Chem.* **1994**, *59*, 1428−1443.

(6) Corey, E. J.; Pyne, S. G. *Tetrahedron Lett.* **1983**, *24* (28), 2821−2824.

(7) For example, see: (a) Sowell, C. G.; Wolin, R. L.; Little, R. D. *Tetrahedron Lett.* **1990**, *31* (4), 485−8. (b) Schwaebe, M.; Little, R. D. *J. Org. Chem.* **1996**, *61* (10), 3240−4. (c) Matsuo, G.; Kawamura, K.; Hori, N.; Matsukura, H.; Nakata, T. *J. Am. Chem. Soc.* **2004**, *126* (44), 14374−14376.

(8) Fry, A. J.; Little, R. D.; Leonetti, J. *J. Org. Chem.* **1994**, *59* (17), 5017−26.

(9) Anderson, J. D.; Baizer, M. M.; Petrovich, J. P. *J. Org. Chem.* **1966**, *31* (12), 3890−7.

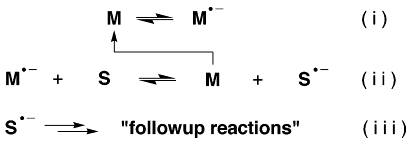
(10) (a) *Organic Electrochemistry*, 4th ed.; Nielsen, M. F., Utley, J. H. P., Lund, H., Hammerich, O., Eds.; Dekker: New York, 2001; pp 795−882 . (b) Moëns, L.; Baizer, M. M.; Little, R. D. *J. Org. Chem.* **1986**, *51* (23), 4497−8. (c) Amputch, M. A.; Little, R. D. *Tetrahedron* **1991**, *47* (3), 383−402.

(11) Lund, H. Simonet, J. *J. Electroanal. Chem.* **1975**, *65*, 205−218.

(12) (a) Schreiber, S. L.; Claus, R. E.; Regan, J. *Tetrahedron Lett.* **1982**, *23* (38), 3867−3870. (b) Schreiber, S. L.; Claus, R. E. *Organic Syntheses;* Wiley & Sons: New York, 1990; Collect. Vol. 7, pp 168−173.

(13) Hon, Y. S.; Chu, K. P.; Hong, P. C.; Lu, L. *Synth. Commun.* **1992**, *22*, 429−443.

SCHEME 3. Mediated Electron Transfer



$$M \rightleftharpoons M^{\bullet-} \quad (i)$$

$$M^{\bullet-} + S \rightleftharpoons M + S^{\bullet-} \quad (ii)$$

$$S^{\bullet-} \longrightarrow \text{"followup reactions"} \quad (iii)$$

substance that serves a role similar to that of a sensitizer in photochemical transformations.[14] In such an experiment, the potential is set at a value where only the mediator, **M**, is reduced or oxidized, as the case may be (Scheme 3). If the overall process to be achieved is a reduction, then the reduced form of the mediator, $\mathbf{M}^{-\bullet}$, serves as an electron-transfer agent toward the substrate, **S**, thereby converting the latter to a radical anion, $\mathbf{S}^{-\bullet}$, and simultaneously regenerating the mediator.

One of the salient features of electromediated processes is that they can occur despite the existence of a thermodynamic hurdle that would seemingly preclude electron transfer between the mediator and substrate. As Fry has written:[15] "At first sight, mediated electron transfer appears to present a thermodynamic paradox, in that the substrate undergoes a redox conversion at a potential lower than that required to effect its direct electrolysis." The key to success is that there be one or more fast follow-up reactions that can drain the equilibrium toward the product.[15b] Of many illustrative examples, we cite two interesting cases, one from Utley's laboratory and the other from Simonet's research group.[16] Utley and coworkers reported a Diels–Alder reaction between electrochemically generated *o*-quinodimethane and maleic anhydride. Maleic anhydride, which is easier to reduce than the quinodimethane precursor, served both as a mediator and a dienophile. The Simonet chemistry featured the use of acenaphthene as a mediator, the reduced form of which served as an electron-transfer mediator to several methylenecyclopropanes. The potential was set at that of the mediator, some 0.2–0.3 V more positive than the peak potential for the reduction of the substrate. Several reviews of the field have been written, and the interested reader is referred to them for additional detail.[14–16]

We selected nickel(II) salen (**15**) since its redox behavior is well defined, and its utility in organic synthesis is well established.[17] We initially imagined a pathway wherein Ni(II) would be reduced to Ni(I) and the latter would serve as an electron-transfer agent toward the substrate. The alternative ligand-centered electron transfer that is also illustrated in Scheme 4 seemed to us to be less likely.[18]

Detailed electrochemical, ESR, and UV–vis studies have been conducted in an effort to differentiate between inner- and outer-sphere electron-transfer options,[19] focusing particularly upon reactions involving alkyl halides.[20] In the literature, one finds that nickel(I) salen complexes **16** react by a metal-centered inner-sphere pathway, while the nickel(II) anion radical **17** functions as an outer-sphere electron donor.[19] This description nicely describes the chemistry of hard electrophiles. We suggest that it should be modified, however, to accommodate the chemistry of the soft electrophiles whose chemistry is described herein (vide infra).

Results

Voltammetry. Cyclic voltammograms were recorded to establish the redox behavior of nickel salen, of the ERC substrate **11**, and of the EHC substrate **14**. As illustrated in Figure 1, nickel(II) salen displays a reversible curve with a cathodic peak potential of −2.1 V versus Ag/$AgNO_3$. The ERC substrate **11**, on the other hand, displays an irreversible curve with a cathodic peak at −2.6 V. Thus, the potential required for the direct reduction of the substrate **11** is 0.5 V more negative than the potential that is to be used to reduce the mediator. Success, therefore, will require that there exist one or more chemical transformations (e.g., protonation, addition of a second electron, cyclization; see Scheme 1 and step iii of Scheme 3) that can shift the equilibrium to the right.[8,11,14–16]

To determine whether redox catalysis was possible, we recorded the cyclic voltammogram of nickel salen in the presence of substrate **11**. As illustrated in Figure 2, there is an increase in current flow, thereby indicating the existence of a so-called "catalytic current", namely, the increase in current that is due to the return of the mediator to the original redox equilibrium in the manner illustrated in Scheme 3.[14]

In accord with the work of Baizer and co-workers,[21] the voltammogram for the EHC substrate **14** displays two poorly resolved peaks, the first at ca. −2.9 V and the other closer to −3.0 V. When the voltammogram for the

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[14] (a) Steckhan, E. *Angew. Chem.* **1986**, *98* (8), 681–99. (b) Simonet, J.; Pilard, J.-F. Electrogenerated reagents. In *Organic Electrochemistry*, 4th ed.; Lund, H., Hammerich, O., Eds.; Dekker: New York, 2001; pp 1163–1225.

[15] (a) Fry, A. J. *Synthetic Organic Electrochemistry*, 2nd ed.; Wiley & Sons: New York, 1989; Chapter 9. (b) In many respects, the situation is similar to acid–base chemistry wherein even though an initial acid–base equilibrium might reside on the left, follow-up reactions can drive the equilibrium toward the product.

[16] (a) Eru, E.; Hawkes, G. E.; Utley, J. H. P.; Wyatt, P. B. *Tetrahedron* **1995**, *51*, 3033–3044. (b) Boujlel, K.; Simonet, J.; Barnier, J.-P.; Girard, C.; Conia, J.-M. *J. Electroanal. Chem.* **1981**, *117*, 161–166.

[17] (a) Gosden, C.; Healy, K. P.; Pletcher, D. *J. Chem. Soc., Dalton Trans.* **1978**, 972–976. (b) Gosden, C.; Kerr, J. B.; Pletcher, D.; Rosas, R. *J. Electrochem. Soc.* **1981**, *117*, 101–107. (c) Dunach, E.; Franco, D.; Olivero, S. *Eur. J. Org. Chem.* **2003**, 1605–1622. (d) Esteves, A. P.; Freitas, A. M.; Medeiros, M. J.; Pletcher, D. *J. Electroanal. Chem.* **2001**, *499* (1), 95–102. (e) Peters, D. G. *Using transition-metal complexes as catalysts for organic electrochemistry*, 226th American Chemical Society National Meeting, New York, Sept. 7–11, 2003; American Chemical Society: Washington, DC, 2003; ORGN-638.

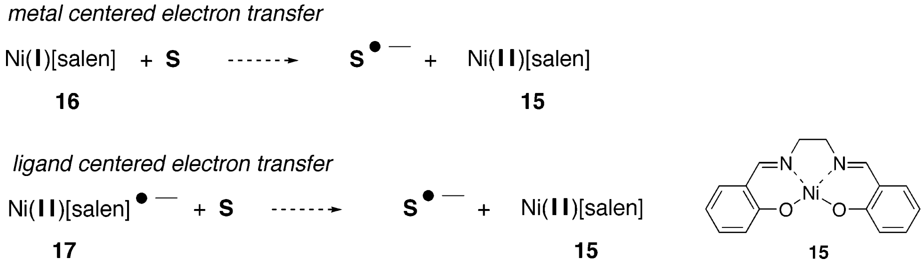
[18] Fielder, S. S.; Osborne, M. C.; Lever, A. B. P.; Pietro, W. *J. Am. Chem. Soc.* **1995**, *117* (26), 6990–3.

[19] (a) Azevedo, F.; Freire, C.; de Castro, B. *Polyhedron* **2002**, *21* (17), 1695–1705. (b) Isse, A. A.; Gennaro, A.; Vianello, E. *Electrochim. Acta* **1992**, *37* (1), 113–118.

[20] Most often, metal salen complexes have been used in electrochemical processes wherein one of the substrates contains an alkyl, aryl, vinyl, allyl, or propargyl halide. This makes sense mechanistically, since the reduced form of nickel can oxidatively insert into the carbon–halogen bond. See ref 16c as well as (a) Condon, S.; Nedelec, J.-Y. *Synthesis* **2004**, *18*, 3070–3078. (b) Nedelec, J.-Y.; Perichon, J.; Troupel, M. Organic electroreductive coupling reactions using transition metal complexes as catalysts. In *Electrochemistry VI: Electroorganic Synthesis: Bond Formation at Anode and Cathode*; Steckhan, E., Ed.; Topics in Current Chemistry 185; Springer: Berlin, 1997; pp 141–173. (c) Alleman, K. S.; Samide, M. J.; Peters, D. G.; Mubarak, M. S. *Curr. Top. Electrochem.* **1998**, *6*, 1–31. (d) Cannes, C.; Condon, S.; Durandetti, M.; Perichon, J.; Nedelec, J.-Y. *J. Org. Chem.* **2000**, *65* (15), 4575–4583. (e) Ozaki, S.; Matsushita, H.; Ohmori, H. *J. Chem. Soc., Perkin Trans. 1* **1993**, (19), 2339–44.

[21] Petrovich, J. P.; Anderson, J. D.; Baizer, M. M. *J. Org. Chem.* **1966**, *31*, 3897–3903.

SCHEME 4. Metal- and Ligand-Centered Electron-Transfer Options



nickel salen redox couple was recorded in the presence of **14**, a substantial catalytic current is observed (see Figure 3). However, an anodic peak is not observed on the return scan despite our attempt to outrun other processes by increasing the scan rate by a factor of 6 viz., to 600 mV/s. This behavior is similar to that of both nickel salen and nickel cyclam complexes when recorded in the presence of alkyl halides.[18] With **14**, the electron-transfer agent, **M**$^{-\bullet}$, is being consumed faster than the rate at which it is oxidized to reform the mediator, **M**. Nevertheless, **M** is being regenerated after delivering an electron to the substrate and at a rate that is sufficiently large to allow the catalytic current to be observed.

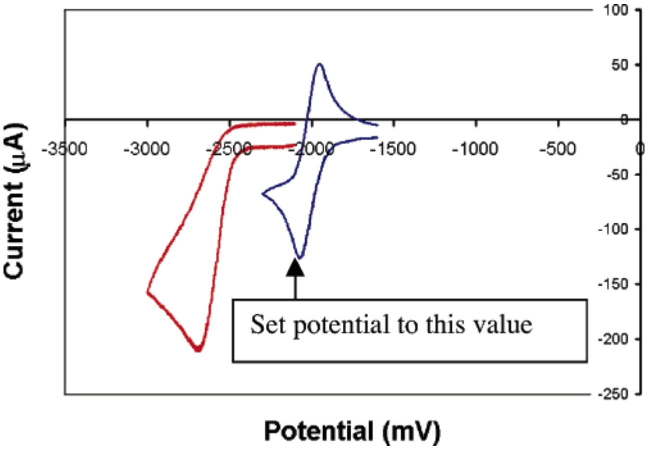


FIGURE 1. Cyclic voltammograms of nickel salen (blue curve) and the ERC substrate, **11** (red curve): 5 mM Ni(salen) in CH_3CN (v = 100 mV/s); 10 mM of the ERC substrate **11** (v = 200 mV/s). RVC cathode, Pt anode, and 0.1 M n-Bu_4NBF_4 in each instance; potentials vs $Ag/AgNO_3$ in CH_3CN.

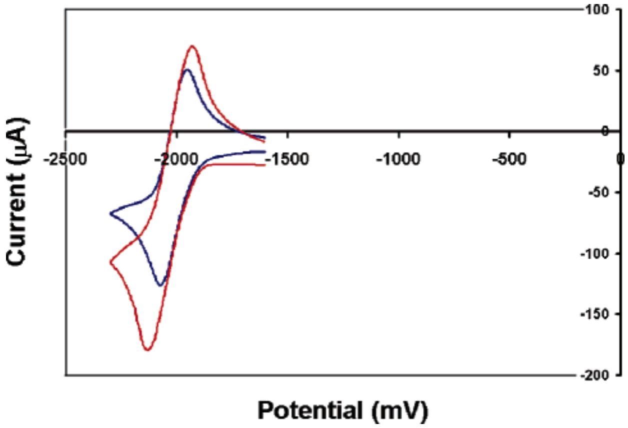


FIGURE 2. Electrocatalysis and reversibility. Cyclic voltammogram of nickel salen (blue curve) and in the presence the ERC substrate **11** (red curve). The blue curve corresponds to 5 mM Ni(salen) in CH_3CN, the red curve to 5 mM Ni(salen) + 40 mM of the ERC substrate **11** in CH_3CN (v = 100 mV/s). RVC cathode, Pt anode, 0.1 M n-Bu_4NBF_4; potentials vs $Ag/AgNO_3$ in CH_3CN.

Preparative Runs. When a solution containing 6 mol % nickel salen (**15**) and the ERC substrate **11** is subjected to a controlled potential of −2.1 V, a value that ensures the direct reduction of the mediator and not the substrate, cyclization occurs; a respectable 72% yield of a mixture of stereoisomeric products **18a/18b**, **c** is produced (see Table 1).[2a] Thus, in accord with expectations based upon the voltammetric results described above, it is possible to affect the ERC reaction electrocatalytically. The methyl ketone **12** behaves similarly and affords a comparable yield of cyclized products **19**. Nitrile **13** proved somewhat more challenging because of the volatility of the product. The difference between the isolated and GC yields of **20** reflect this feature. Gratifyingly, electrohydrocyclization is also achievable electrocatalytically, in this instance to convert dienoate **14** to the vicinal diester **21**. In each instance, reactions were terminated when the starting material disappeared, as evidenced by TLC and GC analysis (5% phenylmethyl silicone capillary column) or by noting when the current dropped to background levels.

To the best of our knowledge, these reactions represent the first instances wherein a nickel salen complex has been used to affect electroreductive cyclizations of this nature.[10a,11] As illustrated in Table 1, cyclizations can be achieved satisfactorily using either a mercury pool or a reticulated vitreous carbon (RVC) cathode. While the yields differ, there is insufficient information to attribute any significance to the variations. Obviously, the RVC electrode is preferred environmentally.

Cobalt(II) Salen as a Possible Mediator. While nickel(II) salen is effective, the analogous cobalt complex, **22**, fails to promote the cyclization of **11**. This is not totally unanticipated, however, given that the reduced form of **22** is a significantly less potent reducing agent.[22] This fact is discernible by comparing the cathodic peak potentials for the nickel(II) salen and cobalt(II) salen redox couples, namely, −2.1 V versus −1.6 V, respectively (compare Figures 1 and 4). Since nickel(II) salen serves admirably as a mediator while cobalt(II) salen does not, we conclude that the 1.1 V barrier between the peak potentials for the cobalt complex (E_{pc} −1.6 V) and **11** (E_{pc} −2.7 V) is too large to allow the transfer to occur from

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[22] (a) Peters, D. G. Halogenated Organic Compounds. In *Organic Electrochemistry*, 4th ed.; Lund, H., Hammerich, O., Eds.; Dekker: New York: 2001; Chapter 8 and references therein. (b) Pletcher, D.; Thompson, H. *J. Electroanal. Chem.* **1999**, *464* (2), 168−175.

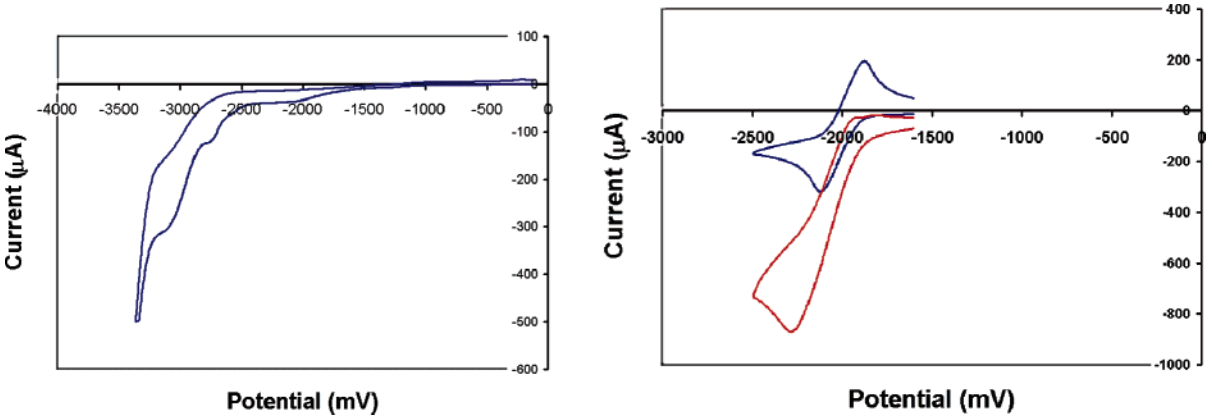
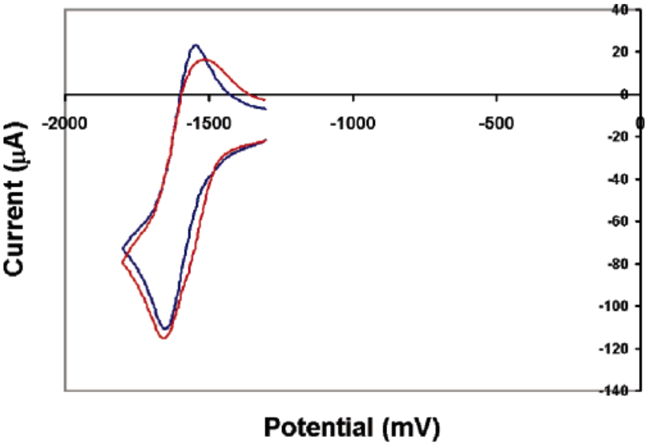


FIGURE 3. Cyclic voltammograms of the EHC substrate **14** (left curve) and nickel salen in the presence the EHC substrate **14** (right). Left side: 40 mM of the EHC substrate **14** in CH_3CN containing 0.1 M n-Bu_4NBF_4 (υ = 200 mV/s). Right side: The blue curve on the right corresponds to 5 mM Ni(salen) in CH_3CN, the red curve to 5 mM Ni(salen) + 40 mM of the EHC substrate **14** in CH_3CN (υ = 600 mV/s). RVC cathode, Pt anode, 0.1 M n-Bu_4NBF_4; potentials vs Ag/$AgNO_3$ in CH_3CN.



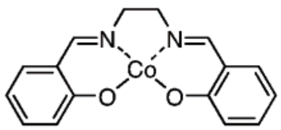


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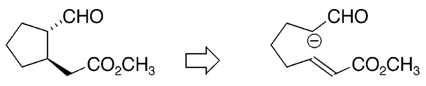
FIGURE 4. Voltammograms of cobalt(II) salen in the absence (blue curve) and presence (red curve) of the ERC substrate **11**. Blue curve: 5 mM cobalt (II) salen in CH_3CN; red curve: 5 mM cobalt(II) salen + 40 mM of ERC substrate **11** in CH_3CN; RVC cathode, Pt anode, 0.1 M n-Bu_4NBF_4 (υ = 200 mV/s); potentials vs Ag/ $AgNO_3$ in CH_3CN.

the reduced form of the cobalt(II) salen to the substrate. This conclusion is borne out by the voltammetric curves shown in Figure 4. Unlike the voltammograms portrayed in Figures 2 and 3 where a catalytic current is readily apparent (vide supra), Figure 4 shows that it is nonexistent when the cobalt(II) salen redox couple is recorded in the presence of the ERC substrate **11**.

Discussion

Electron Transfer and Catalysis. In a beautiful piece of work, Azevedo et al. described the voltammetric properties of a series of nickel complexes, each based upon the parent nickel(II) salen core.[19] By using ESR and UV−vis spectroscopy, the authors concluded that structures possessing an aromatic diimine bridge are reduced to a system that is best described as a radical anion appended to a square planar Ni(II), whereas structures possessing an aliphatic bridge undergo reduction to afford a four-coordinate Ni(I) species, that is, to a metal-centered reducing agent. Consistent with this view, we originally assumed that electron transfer would involve a metal-centered electron transfer from Ni(I) salen to regenerate the mediator and produce the radical anion of the substrate. Several pieces of information generated by us and by other researchers have led us to rethink whether it is the exclusive, or merely a contributing electron-transfer pathway, as it relates to the substrates studied in the present investigation (vide infra).

The first clue that an alternative electron-transfer pathway might be operative, either exclusively or in competition with the metal centered pathway (vide infra), arose when aldehyde **23** was characterized as a side product of the electroreductive cyclization of **11** (~20% yield). Given that **23** is absent from nonmediated electroreductive cyclizations of **11**,[1,2a] we conclude that its formation is linked to the presence of the mediator. Since **23** is simply the product of an intramolecular Michael reaction,[23] we postulate that the reduced form of the mediator must be able to serve as the base that is needed to form the prerequisite enolate **24**. The picture of the electron-transfer agent that begins to emerge, therefore, differs from the one that would associate with a metal-centered species.



23 **24**

Also consistent with an alternative characterization of the intermediate are experiments described by Peters and co-workers.[24] They discovered that the catalytic reduction of 1-iodooctane in the presence of "electrogenerated nickel(I) salen" led to the formation of **25**−**27** (R = n-octyl, Figure 5), each resulting from the alkylation of one or both of the imino bonds of the salen ligand. An erosion of catalytic activity accompanied these events.

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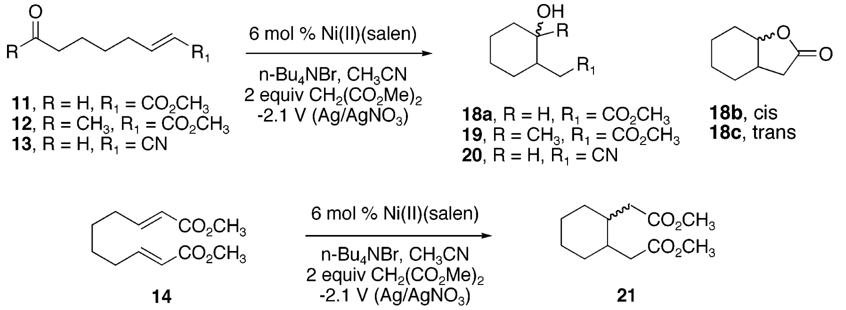
(23) Little, R. D.; Masjedizadeh, M. R.; Wallquist, O.; McLoughlin, J. I. The Intramolecular Michael Reaction. In *Organic Reactions*; Wiley: New York, 1995; Vol. 47, Chapter 2.

TABLE 1. Preparative Scale Mediated ERC and EHC Reactions



substrate	cathode[a]	yield (%)
aldehyde **11**	RVC	**72**[b]
aldehyde **11**	Hg pool	**94**[c]
ketone **12**	RVC	**70**[d]
diester **14**	Hg pool	**60**[e]
diester **14**	RVC	**73**[f]
nitrile **13**	RVC	**40**[g], **70**[h]

[a] In each instance, a Pt anode was used. [b] Trans/cis = 2.6:1. [c] Trans/cis = 2.9:1. [d] Trans/cis = 1.4:1. [e] Trans/cis = 2:1. [f] Trans/cis = 3.1:1. [g] Trans/cis = 3:1, the volatility of the product was confirmed and is presumably the source of the low yield. [h] Yield determined by GC using decalin as an internal satndard for this case only.

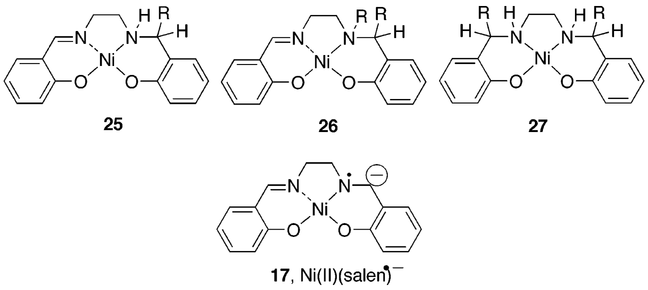
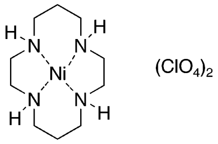


FIGURE 5. Alkylated salens; evidence for ligand involvement.

They concluded that the reactive entity leading to structures **25**−**27** is best described by a ligand-centered species, namely, Ni(II) (salen)$^{-\bullet}$ (**17**). While the reduced form of nickel(II) salen displays an ESR spectrum that shows delocalization of spin onto the ligand,[24a] the isolation of the alkylated adducts **25**−**27** provides compelling evidence for the intervention of such a species.

We suggest that **17** can also account for our results, and that it does so by serving both as a base and as a docking site where an inner-sphere electron transfer to the substrate can occur (see Scheme 5). Thus, the substrate can undergo deprotonation to form the enolate **24** needed for the subsequent intramolecular Michael reaction or conjugate addition leading to **28**. The latter process nicely pairs the electronic characteristics of a soft nucleophile with a soft electrophile. Cleavage of the highlighted bond in **28** releases the requisite radical anion **29**, completes the electron-transfer process, and regenerates the mediator **15**. The ability to conjugately add and then release a modified form of the substrate in a thermodynamically sensible step (**28** to **29**) is what we believe to be the key feature that allows these reactions to proceed catalytically. Thus, the factor that sometimes conspires to make the salen ligand less than ideal as a catalyst for the chemistry of halides (namely, the addition of R−Hal to **17** to afford **25**−**27**) may constitute the most important ingredient needed to affect the catalytic reductive cyclization of substrates such as **11**−**14**.

To test these ideas, we have performed two experiments. In one, we used nickel(II) cyclam (**30**) in place of nickel(II) salen (**15**) and attempted to affect the cyclization of **11**.[25] It did not occur; the starting material was recovered unchanged. Since the cyclam ligand cannot be reduced, an electron transfer would be forced to be a metal-centered process. That cyclization did not occur is, therefore, consistent with but does not demand the existence of the ligand-centered electron-transfer pathway illustrated in Scheme 5.[26]



30

In another, more direct test of our ideas, we synthesized and examined the chemistry of the modified salen complex **31** (Scheme 6).[27] Were the electron transfer a metal-centered event, this simple structural modification of the ligand should have little effect (probably none) upon the chemistry. The redox potential of a solution containing it and the ERC substrate **11** was controlled so that only the mediator **31** could be reduced directly; therefore, the results reflect the role the mediator plays

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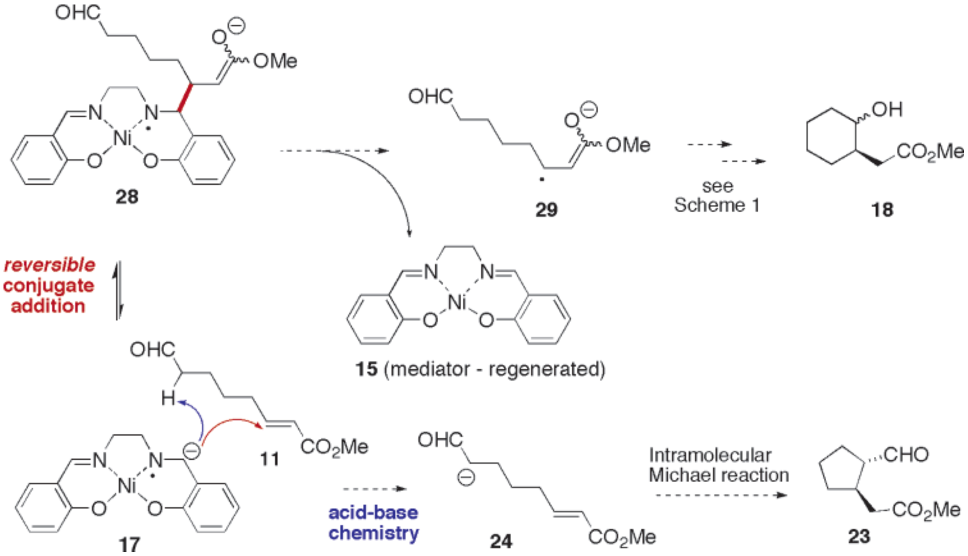
[24] (a) Goken, D. M.; Peters, D. G.; Karty, J. A.; Reilly, J. P. *J. Electroanal. Chem.* **2004**, *564* (1−2), 123−132. (b) Goken, D.; Peters, D.; Tomaszewski, J.; Karty, J.; Reilly, J. *Alkylation of Nickel Salen during Controlled-Potential Electrolyses in the Presence of Alkyl Halides*, Joint International Meeting of the Electrochemical Society, Inc., Honolulu, HI, 2004; Electrochemical Society: Pennington, NJ, 2004; Paper 2124.

[25] Ihara, M.; Katsumata, A.; Setsu, F.; Tokunaga, Y.; Fukumoto, K. *J. Org. Chem.* **1996**, *61* (2), 677−84.

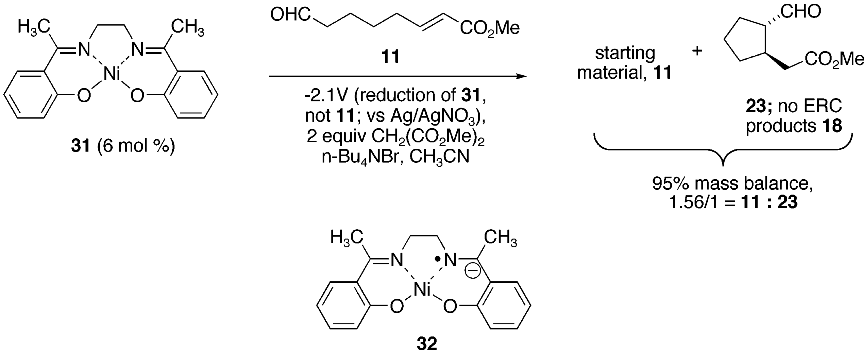
[26] It is possible that the outcome has nothing to do with mechanistic detail shown in Scheme 5 but instead simply reflects that the additional 0.2 V presents a thermodynamic barrier that is too high to be overcome.

[27] (a) Tidjani-R. N.; Djebbar-Sid, S.; Hamrit, H.; Benali-Baitich, O. *J. Soc. Alger. Chim.* **2001**, *11* (1), 121−130. (b) Gilbert, W. C.; Taylor, L. T.; Dillard, J. G. *J. Am. Chem. Soc.* **1973**, *95*, 2477−2482.

SCHEME 5. One Option for the Regeneration of the Mediator



SCHEME 6. The Ligand-Modified Salen 31 Fails as an Electron-Transfer Agent



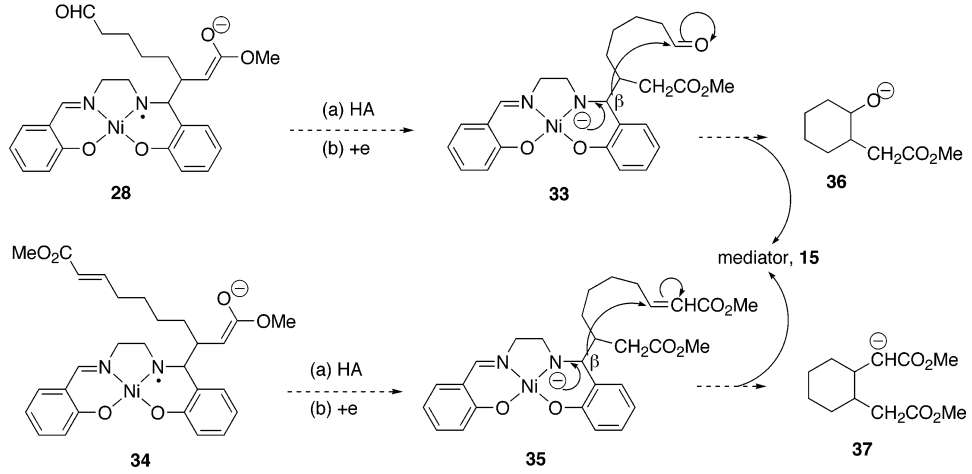
in determining the outcome. They were entirely different from those obtained using the parent nickel salen complex **15**. No electroreductive cyclization products were obtained. Only the intramolecular Michael adduct **23** and the starting enoate were observed (95% mass balance). In addition, there was a substantial decrease in current flow, it being cut in half within the first 15 min. No longer were there the benefits of a catalytic current. The catalyst was being consumed, but how?

We suggest that the methyl groups of the modified ligand increase the congestion about the radical anion **32**, thereby reducing its ability to serve as a nucleophile but not as a base, just as lithium dicyclohexylamide is less nucleophilic than LDA. The radical anion **32**, therefore, is expected to no longer be as effective in the conjugate addition step that is deemed critical to achieve electron transfer. Instead, it can be consumed by serving as a base. Since only 6 mol % of the modified nickel salen complex (**31**) is present per mole of substrate, it should not and does not take long for it to be consumed. Given that the potential is set at that of the nickel salen complex and not that of the substrate, the current would be expected to drop sharply when the complex is consumed. This accords with observation.

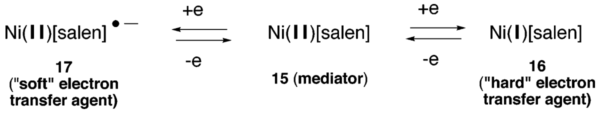
Mechanistic Alternatives. One possibility posits that instead of expelling the radical anion **29** from the ligand to regenerate the mediator **15** in the manner shown in Scheme 5, the intermediate formed after the initial conjugate addition step, namely, **28**, rapidly picks up a proton and then a second electron to afford the nitrogen-centered anion **33** shown in Scheme 7.[8] This would be consistent with the known mechanism for the ERC reaction when it is conducted in the absence of a mediator.[8] We suggest that the regeneration of the mediator could occur in concert with cyclization between the β-carbon and the remotely tethered acceptor unit. At this point, differences between the possible fate of the intermediates **33** and **35**, derived from **28** and **34**, respectively, become apparent. Each process sees one species converted to two and is therefore entropically favorable, and each allows the conjugation between the aromatic unit and the C−N π-bond of the salen core to be reestablished, and each establishes a new C−C σ-bond at the expense of the σ -bond that attaches the substrate to the ligand. The difference between the two resides in the nature of the anion that would be formed as a consequence of the cyclization. For **35**, this leads to enolate **37**, that is, to a delocalized entity, whereas a nonstabilized oxyanion **36** is formed as a result of the cyclization of **33**. The former event is obviously thermodynamically more favorable than the latter.

Concluding Remarks and Future Prospects. Indirect spectroscopic evidence in support of the ligand-centered radical anion hypothesis is found in the ESR studies of Cros and co-workers.[28] They were able to demonstrate that “Without any doubt, the two species

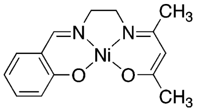
SCHEME 7. Mechanistic Alternative and Possible Origin of Additional Catalytic Current



SCHEME 8. Equilibrium Involving Ligand- and Metal-Centered Reduced Forms



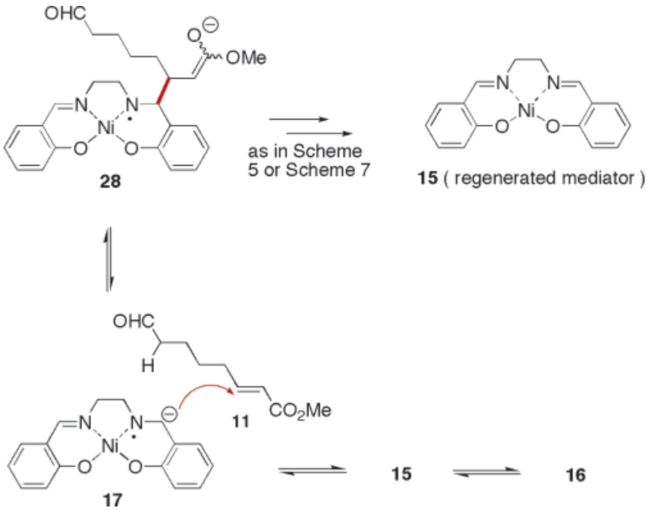
observed during the early stage of the electrolysis of NiAESalen (**38**) are actually the corresponding nickel(I) complex and the nickel(II)-stabilized radical anion." They go on to write, "Since the radical is no longer discernible at the end of the reduction process, we may reasonably assume the occurrence of rapid ligand-to-metal electron transfer."



38, NiAESalen

We too realize that our results do not preclude the existence of more than one electron-transfer pathway. There could be, for example, equilibrium between a metal-centered redox couple (viz., between **15** and **16**) and one that is centered on the ligand (**17**; note Scheme 8).[29] This scenario allows for the existence of a mechanistic continuum wherein depending upon the substrate being investigated, one form may be more prominently involved with the chemistry than another. It is reasonable, for example, that hard alkyl halide electrophiles will (and do) react preferentially, but not exclusively,[20] at the metal since it is the hardest site in the reduced species. It seems equally reasonable to suggest that the soft electrophiles studied in the present investigation should react at the softest site in the reduced species, namely, on the ligand, as illustrated in Scheme 5.

SCHEME 9. Matching Soft Nucleophile with Soft Acceptor; Shifting Equilibria Involving Reduced Nickel(II) Species 15−17



We believe that the ERC and EHC substrates described in this paper allow the radical anion character of the reduced nickel(II) salen complex **17** to be expressed by properly matching its electronic characteristics with that of the acceptor. Thus, the conjugate addition of radical anion **17** to enoate **11** matches a soft nucleophile with a soft electrophile. Once a substrate embarks upon the pathway shown in Scheme 9, then the subsequent release of the mediator **15**, be it via the pathway depicted in Scheme 5 or Scheme 7, drives the equilibria involving **15**−**17** toward **17** and further guarantees its involvement.

We intend to investigate the course of both the ERC and EHC reactions using spectroelectrochemical techniques, focusing particularly upon the use of ESR spectroscopy, a technique we have previously used successfully to characterize the reactive intermediates formed in the reduction of nitroalkenes.[30] Of special interest, of course, will be the detection of intermediates such as **28** and **29**, since they are postulated to play a key role in the chemistry and because their detection would provide

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[28] Cros, G.; Costes, J.-P.; De Montauzon, A. *Polyhedron* **1984**, *3* (5), 585−588.

[29] A reviewer has made the reasonable suggestion that the proposed equilibrium could be reformulated as a molecular orbital argument involving electron density redistribution. We agree but delay doing so until we obtain evidence to favor one viewpoint over another. In some respects, we have already incorporated aspects of a molecular orbital description by suggesting that the nature of the electron-transfer agent can vary in response to the electronic requirements of the substrate.

[30] Mikesell, P.; Schwaebe, M.; DiMare, M.; Little, R. D. *Acta Chem. Scand.* **1999**, *53* (10), 792−799.

exceptionally strong evidence to support or speak against our mechanistic hypotheses. We are also interested in extending this chemistry to catalytic asymmetric processes and will report our findings as the research unfolds.

Experimental Section

Cyclic Voltammetry. A single compartment cell, constructed from a simple glass vial, was used for the cyclic voltammetry experiments. A vitreous carbon working electrode was used (surface area: 0.033 cm^2); a platinum wire was used as counter electrode (surface area: 0.6 cm^2). The potentials were recorded against the reference of Ag/0.01 M $AgNO_3$ immersed in acetonitrile containing 0.1 M n-Bu_4NBF_4 and was separated from the medium by a Vycor membrane. This electrode has a potential of +0.35 V versus the aqueous saturated calomel electrode (SCE).[31] The solution was deoxygenated for at least 10 min by bubbling argon, and the cell contents were maintained under an argon atmosphere during the experiment. Polishing solution (alumina) and water was used to clean the working electrodes after use. Cyclic voltammetry (CV) was performed using a computer-controlled potentiostat. The data were collected and exported to a spreadsheet program.

General Procedure for Preparative Catalytic Electrolysis. All reactions were carried out in an H-cell with a platinum anode and a Ag/0.01 M $AgNO_3$ reference electrode. This electrode has a potential of +0.35 V versus the aqueous saturated calomel electrode (SCE) at 25 °C.

A 0.1 M solution of n-Bu_4NBr in CH_3CN (20 mL) was poured over a pool of Hg (9 cm^2 surface area) in the cathodic compartment of a divided cell, equipped with a reference electrode. The tip of the reference electrode was 1.0 cm from the surface of the cathode, and a stirbar was placed on top of the Hg pool. When a reticulated vitreous carbon (RVC) electrode was used, it was inserted into the cathodic chamber; the reference electrode was positioned ~2 mm from the cathode. To the anode chamber was added a stirbar and 20 mL of a 0.1 M solution of n-Bu_4NBr. The anode consisted of a square, flat platinum surface (4 cm^2 surface area). Cyclohexene (0.5 mL) was added to the anode chamber to trap the Br_2 generated at the anode from the oxidation of bromide found in the supporting electrolyte n-Bu_4NBr. Both chambers were degassed with Ar gas for 20 min. A pre-electrolysis potential of −2.1 V was applied, and the current was monitored until a constant value of 0.2 mA was observed. In a separate 25-mL round-bottom flask, a 0.02 M solution of **11** (200 mg, 1.176 mmol) was prepared in a solution also containing 0.1 M n-Bu_4NBr. To this solution was added 22 mg of Ni(II) salen (6 mol %, 0.071 mmol). This solution was degassed for 20 min. The solution was a dark red.

After the pre-electrolysis, the current was stopped, a solution containing the substrate was added to the cathodic chamber via syringe, and the catholyte chamber was placed under an Ar atmosphere. The current flow was resumed by applying a potential of −2.1 V. Immediately, the current rose to −35 mA. The catholyte solution gradually turned a dark blue color over the next 2 h. TLC and GC analysis indicated the disappearance of starting material after 4 h and the coulometer indicated that 2 F/mol of charge had passed.

The electrolysis was stopped and the catholyte was transferred to a round-bottomed flask. The catholyte was concentrated via rotary evaporation. The slurry was taken up in water (20 mL) and was extracted with Et_2O (3 × 25 mL). The combined organic layers were washed with brine (3 × 25 mL) and were dried over $MgSO_4$. The solvent was removed in vacuo to give the crude product, which was purified by flash chromatography.

(*E*)-8-Oxo-oct-2-enoic Acid Methyl Ester (11). 6,6-Dimethoxyhexanal[12] (5.0 g, 31 mmol) was dissolved in 65 mL of CH_2Cl_2 and (carbomethoxymethylene)triphenylphosphorane (25.0 g, 77.5 mmol) was added in one portion at room temperature. The reaction mixture was stirred for 3.5 h, and TLC analysis (30% Et_2O in petroleum ether) indicated that conversion to the unsaturated ester was complete. A solution of trifluoroacetic acid (8 mL) and water (75 mL) was added to form a biphasic mixture. The reaction was monitored by TLC (30% Et_2O in petroleum ether), and upon completion of hydrolysis of the acetal (3 h), the organic phase was separated. The organic phase was washed with saturated aqueous $NaHCO_3$ (6 × 100 mL) and water (3 × 75 mL) and was dried over $MgSO_4$. Upon removal of the solvent under reduced pressure, the crude oil was purified by column chromatography over silica gel (30% Et_2O in petroleum ether) to give the title compound (4.06 g, 23.87 mmol, 77% yield) whose spectral data matched those reported previously.[2a]

8-Oxo-(E)-non-2-enoic Acid Methyl Ester (12). A solution of aldehyde **11** (0.305 g, 1.79 mmol) in THF (10 mL) was cooled to −78 °C. To this solution was added methyllithium (1.17 mL of a 1.6 M solution in hexane, 1.88 mmol). The reaction was monitored for the disappearance of starting material by TLC (50% Et_2O in petroleum ether). After 3 h, the solution was warmed to 0 °C and then was immediately quenched with 30 mL of brine. The aqueous layer was extracted with CH_2Cl_2 (4 × 10 mL), and the combined organic layers were dried with $MgSO_4$. The solvent was evaporated in vacuo to give the known alcohol.[32] IR (neat) 3422, 2930, 2858, 1722, 1655, 1436, 1271, 1196, 1040, 974, 909, 714 cm^{-1}. The alcohol (0.33 g, 1.79 mmol) was dissolved in DMSO (3.57 mL) and CH_2Cl_2 (5 mL) and was cooled to 0 °C. To this solution was added triethylamine (1.26 mL, 0.95 mmol), and the solution was stirred for 2 min. SO_3·pyr complex (1.42 g, 8.95 mmol) was added in one portion and the solution was stirred for 1.5 h. After 1.5 h, 50 mL of water was added, the solution was washed with diethyl ether (3 × 20 mL), and the combined organic layers were dried over Na_2SO_4. The solution was concentrated in vacuo to give the crude ketone, a known substance,[5] which was purified by column chromatography (50% Et_2O in petroleum ether) to give **12** (0.27 g, 0.95 mmol, 53% yield). IR (neat) 2947, 1716, 1656, 1436, 1272, 1197, 1175, 1038, 983, 915, 730 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.93 (dt, J = 6.8, 15.6, 1H), 5.80 (dt, J = 1.6, 15.6, 1H), 3.64 (s, 3H), 2.4 (m, 2H), 2.2 (m, 2H), 2.05 (s, 3H), 1.6 (m, 3H), 1.4 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 208.7, 167.1, 149.1, 121.3, 51.5, 43.4, 32.0, 27.5, 23.2, 21.5.

(E)-8-Oxo-oct-2-enenitrile (13). A suspension of NaH (0.71 g of 60% in mineral oil, 18.6 mmol) in dry THF (27 mL) was cooled to 0 °C over an ice bath. Diethyl (cyanomethyl)-phosphonate (2.96 mL, 18.6 mmol) was added dropwise via syringe. The reaction mixture was warmed to room temperature and was stirred for 1 h after which time hydrogen gas evolution had ceased and the suspension had become a homogeneous solution. 6,6-Dimethoxyhexanal[12] (2.0 g, 12.4 mmol) was dissolved in THF (5 mL) and was transferred to the reaction vessel dropwise at room temperature. After 3 h, TLC (30% Et_2O in petroleum ether) indicated that conversion to the unsaturated nitrile was complete. The reaction was concentrated in vacuo, and the crude mixture was dissolved in CH_2Cl_2 (30 mL) and a solution of trifluoroacetic acid (3.2 mL) and water (40 mL) was added to form a biphasic mixture. The reaction was stirred overnight. The organic layer was separated and then was washed with $NaHCO_3$ (3 × 15 mL) and brine (3 × 15 mL) and was dried over $MgSO_4$. The solvent was evaporated, and the crude product was purified by column chromatography (50% Et_2O in petroleum ether) to afford the (*E*)-isomer **13** in a 78% yield (1.325 g, 9.67 mmol). The spectral data matched those reported previously.[33]

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(31) (a) Fry, A. J.; Fry, P. F. *J. Org. Chem.* **1993**, *58* (13), 3496−3501. (b) Moe, N. S. *Anal. Chem.* **1974**, *46*, 968.

(32) Hanessian, S.; Dhanoa, D. S.; Beaulieu, P. L. *Can. J. Chem.* **1987**, *65* (8), 1859−1866.

***trans*-(2-Hydroxycyclohexyl)-acetic Acid Methyl Ester (18a), *cis*-Hexahydro-benzofuran-2-one (18b), *trans*-Hexahydro-benzofuran-2-one (18c).** (*E*)-8-Oxo-oct-2-enoic acid methyl ester **11** (200 mg, 1.18 mmol) was transformed into the cyclized hydroxy ester **18a**, the cis lactone **18b**, and the trans lactone **18c** according to the general procedure for preparative scale runs described above. The crude product consisted of a yellow oil (192 mg, 1.11 mmol, 94% yield when a Hg cathode was used; 146 mg, 0.85 mmol, 72% yield using an RVC cathode). The oil was purified by chromatography on silica gel (30% Et_2O/ petroleum ether) to give the three products **18a**, **18b**, and **18c** in a trans/cis ratio of 1:0.34. The ^{1}H NMR data matched those reported previously.[28,34]

***trans*-(2-Formylcyclopentyl)-acetic Acid Methyl Ester (23).** The intramolecular Michael addition product **23**, isolated in a 25% yield (0.28 mmol) when an RVC cathode was used, displayed the following characteristics: TLC R_f 0.25 (SiO_2, 30% Et_2O/petroleum ether), vanillin; IR (neat) 2952, 2870, 2718, 1720, 1436, 1247, 1194, 1175, 1010, 916, 851, 731 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.61 (d, J = 3.1 Hz, 1H), 3.65 (s, 3H), 2.58 (m, 1H), 2.45 (m, 2H), 1.98 (m, 1 H), 1.9 (m, 2H), 1.7 (m, 2H), 1.3−1.2 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 203.4, 173.1, 57.6, 51.8, 39.1, 37.3, 33.0, 26.9, 24.9. The ^{1}H NMR and IR data matched those reported previously.[35]

(2-Hydroxy-2-methyl-cyclohexyl)-acetic Acid Methyl Ester (19). Methyl ketone **12** (268 mg, 1.45 mmol) was transformed into the cyclized hydroxy ester **19** by following the general procedure described above. The crude product was isolated and purified by chromatography on silica gel (30% Et_2O/petroleum ether) to give the *cis*-hydroxy ester **19a** and the *trans*-hydroxy ester **19b** (189 mg, 1.01 mmol, 70%, 0.71/1.00 trans/cis). The ^{1}H NMR data matched those reported previously.[5]

(2-Hydroxy-cyclohexyl)-acetonitrile (20). Nitrile **13** (0.118 g, 0.855 mmol) afforded a 1.0/3.0 mixture of cis/trans diastereomers as a colorless oil, after following the general procedure using an RVC cathode. The crude material was purified by chromatography on silica gel (30% Et_2O/petroleum ether) to afford a 40% yield (0.048 g, 0.345 mmol) of **20**. The proton NMR and IR data matched that previously published for the cis and trans isomers.[28] LREI-MS m/z 138, 122, 110, 95, 83, 70, 54; HRMS (CI/CH_4) (calcd for $C_8H_{14}NO + H$) 140.107539, found m/z 140.1080 $(M+H)^+$.

The volatility of the product was demonstrated by evaporating a solution of the product dissolved in $CDCl_3$ using a rotary evaporator and a water bath temperature of 40 °C. The product was found in the distillate (confirmed by TLC). This prompted another preparative run using Decalin (mixture of cis/trans isomers) as an internal standard. The single-point internal standard method was followed. A response factor of 0.323 was determined and was used to calculate the amount of product obtained. Thus, nitrile **13** (0.060 g, 0.434 mmol) afforded 0.042 g (0.3 mmol, 70% yield) of cyclized material as characterized by GC/MS. The retention time of the cyclized product was 15.28 min, using the following conditions: 30 m 5% phenyl-methyl silicone capiliary column, initial temperature 40 °C, temperature ramp 10 °C/min, final temperature 300 °C.

(2-Methoxycarbonylmethyl-cyclohexyl)-acetic Acid Methyl Ester (21). Dimethyl (*E*,*E*)-2,8-decadienedioate[13] **14** (200 mg, 0.883 mmol) afforded a mixture of diastereomers **21** (cis/trans 0.5/1.0) as a colorless oil after following the general procedure described above. The crude material was purified by chromatography on silica gel (30% Et_2O/petroleum ether) to afford **21** in a 60% yield (120 mg, 0.53 mmol). This compound has been synthesized previously.[36] The following data is for the trans isomer: TLC R_f 0.13 (SiO_2, 30% Et_2O in petroleum ether; vanillin stain); IR (neat) 2924, 2854, 1733, 1435, 1159, 1011 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.65 (s, 6H), 2.49 (dd, J = 3.8, 14.7, 2H), 2.19 (dd, J = 8.5, 14.9, 2H), 1.6−1.8 (m, 6H), 1.25 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.8, 51.7, 39.2, 32.6, 29.9, 25.9; LREI-MS m/z 197, 170, 155, 139, 123, 95, 74, 59, 41; ESI+-TOF m/z 229 $(M+H)^+$, 251 $(M+Na)^+$; HRMS (calcd for $C_{12}H_{20}O_4 + Na$) 251.1253, found 251.1245.

Acknowledgment. We are pleased to acknowledge support from the Petroleum Research Foundation (PRF No. 43443-AC1) of the American Chemical Society and the U.S. National Science Foundation (CHE-0200855).

JO051148+

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(34) Fox, D. P.; Little, R. D.; Baizer, M. M. *J. Org. Chem.* **1985**, *50* (12), 2202−2204.

(35) Crabbe, P.; Cervantes, A.; Guzman, A. *Tetrahedron Lett.* **1972**, *13*, 1123−1125.

(36) Nelson, N. A.; Paquette, L. A. *J. Org. Chem.* **1962**, *27* (6), 2272−2274.